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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,114	08/04/2003	Gary D. Glick	UM-08192	6392

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EXAMINER	
EBRAHIM, NABILA G	

ART UNIT	PAPER NUMBER
1618	

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07/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/634,114	GLICK, GARY D.	
	Examiner	Art Unit	
	NABILA G. EBRAHIM	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 12-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 12-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/30/2008, 05/30/2008, 11/14/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1, 12-21 are pending in the application.

Status of Office Action: non-final

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

In view of amending the claims, the rejection of claim 12 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is hereby withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 1, and 12-21 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al (Synthesis of 3-Substituted 1, 4-Benzodiazepin-2.ones, Braz. Chem., foc., Vol. 9, No. 4, 375-379, 1998. **provided by Applicant in the IDS dated 4/6/05**); (hereinafter Kim) in view of Punegova et al. RU 2096044 (abstract), and further in view of Soykan et al. US 6824561 (Soykan).

Kim teaches a novel BZ-423 compound that is benzodiazepine analog, see abstract. the reference teaches the recited compound is sharing all the pharmacological activities with benzodiazepine, see page 375.

Kim does not disclose the use of the disclosed compounds in a stent.

Punegova teaches melatonin based implant composition for controlling biological rhythm in animals. The composition comprises (in wt %): 10-40 melatonin, 55.5-89.95 Tsiakrin-EO (ethylcyanoacrylate-based polymer), 0.05-4.5 plasticiser (phthalate, alkylcyanoacetate or triacetin). A psychotropic drug e.g. phenothiazine or benzodiazepine derivatives is optionally included in an amount of 7-25 wt%. Note that stent are types of implants (as evidenced by Kullinan et al. US 6147092 who teaches that an example of local delivery by an implant is the use of a stent. Stents are designed to mechanically prevent the collapse and reocclusion of the coronary arteries. Incorporating a pharmaceutical agent into the stent delivers the drug directly to the proliferative site, see col. 11, lines 16+).

It would have been obvious to one of ordinary skill in the art to deliver the compound recited in claim 1 (Bz-423) in a stent because Punegova teaches that Benzodiazepine derivatives can be included in an implant which can be a stent. It would have been obvious because a person of ordinary skill has good reason to try different and recently known derivatives of Benzodiazepines for elution in a stent, it is likely that bz-423 in a stent is not innovative but of ordinary skill and common sense.

Neither of the references teaches delivering the combinations of the drugs recited in the instant claims through the stent.

Soykan teaches implantable system with drug-eluting cells for on-demand local drug delivery. The imlpantable system is a stent comprising a composition which in turn comprises drugs such as nitric oxide, prostaglandin H synthase (to restore an endogenous inhibitor of platelet aggregation and vasoconstriction (col. 9, lines 31+), antiplatelets (col. 10, line 27), anti-inflammatory (col. 12, line 4). The reference discloses that it was known in the art to use stents for delivering a drug e.g., antiplatelet agents, anticoagulant agents, antimicrobial agents, antimetabolic agents (col. 1, lines 56+) and also that stents seeded with autologous endothelial cells were known in the art since the year 1989 (col. 2, lines 12+).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine any of the drugs disclosed by Soykan with the benzodiazepine compound recited in claim 1 to enhance the effect of the drug comprised in the stent implanted according to the condition being treated. The skilled artisan would expect success since these drugs were known previously in the art to be effective when delivered from a stent. Accordingly, the whole invention was prima facie obvious to one of ordinary skill in the art.

Regarding the amendments to instant claim 1 which recites “a mitochondrial oligomycin sensitivity conferring protein component in a mammalian subject; wherein said pharmaceutical composition comprises an agent capable of binding a mitochondrial oligomycin sensitivity conferring protein component, wherein said agent does not bind to a central benzodiazepine receptor and binds only with low affinity to a peripheral benzodiazepine receptor”. The amendments represent a functional property of the composition. Since the composition was properly rejected as being obvious over Kim in view of Punegova and further in view of Soykan,

then the combination of the teaching of the three references would have been capable of performing the said function.

Regarding new claim 21 which recites that the mammalian subject is a human, it is noted that the generic disclosure of Punegova of "a based implant composition for controlling biological rhythm in animals" does not exclude humans.

Accordingly, claims 1, 12-21 are still properly rejected.

Response to Arguments

1. Applicant's arguments filed 4/4/2008 have been fully considered but they are not persuasive. Applicant argues that:

- Amended Claim 1 requires that the agent, i.e., the compound is, "capable of binding a mitochondrial oligomycin sensitivity conferring protein component." Neither the Kim reference, Punegova abstract, nor the Soykan patent teach or recognize that certain benzodiazepine compounds (e.g., the compound) could bind to a mitochondrial oligomycin sensitivity conferring protein component. The Applicant's discovery that certain benzodiazepine compounds bind to the oligomycin sensitivity conferring protein, and that such a binding causes increased superoxide levels is a significant advance because, as explained in Applicant's patent application, cell death results from the increase in superoxide levels. Applicant also argues that None of the references cited by the Examiner describe the binding activity of the agent specified in Claim 1.

To respond: the amendments represent a functional property of the composition. Since Kim teaches the compound, Punegova teaches the use of benzodiazepines in implants, and Soykan teaches drug-eluting cells for on-demand local drug delivery such as such as nitric oxide, prostaglandin H synthase (to restore an endogenous inhibitor of platelet aggregation and vasoconstriction (col. 9, lines 31+), antiplatelets (col. 10, line 27), anti-inflammatory (col. 12, line

4)., then the combination of the teaching of the three references would have been capable of performing the said function.

Conclusion

2. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NABILA G. EBRAHIM whose telephone number is (571)272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nabila G Ebrahim/
Examiner, Art Unit 1618

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618